A cross-cultural comparison of the role of some psychosocial factors in the etiology of coronary heart disease : follow-up to the Kaunas-Rotterdam Intervention Study (KRIS)

Chapter 9

SUMMARY

9.1 History and Aims of the KRIS Follow-up Study

In the late 1960s the World Health Organization initiated a feasibility study on the problems of general methodology of large scale intervention studies of CHD. From the point of view of the future applicability of the results it was considered particularly relevant that the study be conducted by centers located in countries with different health service systems. The Kaunas Medical Institute (Kaunas, formerly Lithuanian SSR) and the Rotterdam Municipal Health Center together with the Erasmus University (Rotterdam, The Netherlands) were selected as the participating centers. Hence the name of the study: Kaunas-Rotterdam Intervention Study (KRIS).

The data collection started in March 1972 and ended in December 1974. In each city a sample of 4000 men between 45 and 59 years of age and representing various socioeconomic strata of an urban population was identified. These men were interviewed at the baseline survey, and invited to participate in a screening examination (Glasunov et al., 1981). In Kaunas 2452 (69%) and in Rotterdam 3365 (87%) of the invited men participated in the screening. At the baseline survey or screening information was collected regarding a large number of biological, lifestyle, and psychosocial risk factors.

Both centers separately collected information about the occurrence of cardiovascular events during a ten-year follow-up. In Kaunas the participants were followed by means of a mortality and MI register covering the whole population of Kaunas. In Rotterdam follow-up data were collected by inspection of death certificates and by a questionnaire sent in March 1982 to all surviving participants. This questionnaire was returned by 91% of the participants. Discharge letters of cardiologists and archives of general practitioners were used to verify the medical history of those with heart disease. Both centers made use of this database to do some longitudinal investigations of the determinants of CVD or other diseases.

In 1988 both teams decided to cooperate in the analysis of the ten-year follow-up data. The desirability of a common follow-up study originated from some unique properties of the KRIS: the unusual amount of psychological and sociological information collected, the opportunity to cross-validate the predictive power of some supposedly behavioral risk factors in populations living in different socioeconomic conditions and facing an increase (Lithuania) and a decrease (The Netherlands) of CHD incidence. Therefore, the emphasis of the KRIS follow-up study was laid upon socioeconomic and psychological factors.

9.2 Prevalence of Risk Factors and Indicators

At screening some minor and some major differences between the cohorts were observed. Significant differences were observed in mean age (52 and 53 years in Kaunas and Rotterdam, respectively), mean diastolic blood pressure (88 and 80), mean body mass index (27 and 26), mean cholesterol level (193 and 201), mean glucose tolerance (146 and 165), smoking (subjects who "never-smoked": 27% and 8%), alcohol consumption (subjects classified as "immoderate": 31% and 15%), mean physical activity (Reiff score 209 and 151) and a positive family history of CVD (parents 32% and 40%; siblings 4% and 14%). No differences were observed in systolic blood pressure (138).

At screening, information was collected about the educational and occupational level of the participant, his wife, parents and parents-in-law. The level of education and the occupational status were measured differently in each cohort. Therefore, the distributions were hard to compare.

Both cohorts differed in some other social characteristics. Lithuanian men were more often married and had a more extended social network. Almost none of the Lithuanian participants was born in Kaunas, while half the Dutch participants had always lived in Rotterdam.

Kaunas participants showed somewhat more signs of the coronary prone type A behavior on form N of the JAS. This difference was not significant. Unfortunately enough, it was not possible to compare the cohorts on the Reeder stress scale, because a response set was found to bias the Lithuanian data.

A striking difference between the cohorts was observed in the average perception of their health status. The participants rated their health on a semantic differential test for "my health" and on two direct questions: "How would you assess your own health?" and "What do you think of your own health compared to that of other men of your age?" Factor analysis of the semantic differential test showed that this test measured a general evaluation of health and the extent to which subjects worried about their health. Remarkable differences were observed between the cohorts. More Rotterdammers than Kaunasians considered themselves in good health and they also worried less about their health. Of the participants 16% in Rotterdam and 63% in Kaunas rated their health as poor. Thirty-one percent of the Lithuanians thought their health status was worse than that of other men, compared to 14% in Rotterdam.

9.3 Incidence of Main Endpoints

The biological, lifestyle, and psychosocial factors were related to: (1) all-cause mortality, (2) mortality caused by all CVD, including CHD and cerebrovascular disease (ICD code 390-459), (3) mortality due to CHD (ICD code 410-414), (4) nonfatal MI. The number of deaths due to all causes per 10,000 person years was 146.37 in Kaunas and 121.73 in Rotterdam. Corresponding numbers for mortality due to CVD were 54.59 and 55.99. The number of CHD deaths was 32.85 and 43.47,

respectively. Cumulative incidence of nonfatal MI in Kaunas was 3.6% and in Rotterdam 4.3%. This points to a higher incidence of CHD in Rotterdam. Other analyses revealed that the higher all-cause mortality risk in Kaunas was a result of higher risks of mortality due to external causes (accidents, suicide), stomach cancer, cerebrovascular disease, infectious diseases, and respiratory diseases. Modern diseases, such as CHD and lung cancer, were higher in the Dutch part of the KRIS.

9.4 Impact of Risk Factors and Indicators

Smoking was found to increase the risk for all endpoints in both cohorts. A high cholesterol level was associated with increased risks of the three cardiovascular endpoints in both cohorts. Elevated systolic blood pressure increased the risk for all endpoints in Kaunas and for all-cause mortality and CVD mortality in Rotterdam. An impaired glucose tolerance was positively associated with all endpoints in both cohorts. However, the strength of the associations did not reach conventional levels of statistical significance for CHD mortality in either cohort nor for all-cause mortality and nonfatal MI in the Dutch cohort. The body mass index was found to increase the risk of CVD and CHD mortality in both cohorts. This effect disappeared after adjusting for blood pressure. Generally, protective effects were found for alcohol consumption. Apart from moderate drinking and all-cause mortality in The Netherlands, these effects were, however, never significant in the multivariate models. As for physical activity, rather small effects were observed. Data about changes in risk factor levels were available for Kaunas only. Changes in blood pressure and cholesterol level contributed to the increased risk of all-cause mortality. A change in diastolic blood pressure was a significant predictor of CHD mortality.

A positive history of CVD of one of the parents was not associated with all-cause mortality or CVD mortality. However, in both cohorts, a parental history of CVD increased the risk of nonfatal MI. Due to small numbers it was impossible to compute the risk due to having a sibling with a positive cardiovascular history in Kaunas. The Dutch data showed that having a sibling who suffered from CVD doubled the risk for all cardiovascular endpoints. Having a sibling with cardiovascular history seems to bear more risk than having a parent who suffered from heart disease. The elevated cholesterol level of those who had a parent and a sibling with a positive history of CVD may suggest genetic influences. Taking the cholesterol level and all other risk factors into account, however, hardly changed the relative risks. Therefore, the data suggest that sharing a family culture and a common environment might be at least as important as sharing genes.

The importance of family culture was also suggested by the analysis of the educational level of spouses. The educational level of the participant himself was not associated with any of the endpoints, except all-cause mortality in Rotterdam. The mortality risk was increased by 50% among Dutch participants with an intermediate or low educational level. However, the educational level of a participant's wife was significantly associated with his longevity in both cohorts. The excess mortality risk

of having a wife with a low educational level (age and the educational status of the participant taken into account) was 57% in Kaunas and 115% in Rotterdam. The biological and lifestyle risk factors only partially accounted for this excess mortality risk. Therefore, the data strongly suggest that yet unknown cultural factors associated with a wife's educational level influence the health of her husband. Further explorations of the family background suggested that the educational level of the parents-in-law might be involved in this cultural context as well.

The finding that, in both countries, the wife's educational status has an independent influence upon the longevity of her husband raises a number of questions that deserve further scientific attention. A wife has a strong influence on the lifestyle of a family. We do not know which elements of the total lifestyle are important. Diet and smoking do not account for it completely; the association remained significant when smoking and cholesterol levels were taken into account. Other factors such as general hygiene, use of health care, sleeping habits, and the way in which financial and educational problems are dealt with may be important too. The role of the family, its culture and values, and ways of communication in a family deserve more attention than they actually receive. Studies of coronary patients indicate that they generally experienced more problems at home than at work (Falger, 1989). The observation that having a sibling with a positive history of CVD bears more risk than having a parent with a positive history points in the same direction. Therefore, we recommend encouraging investigations of the influence of the "family culture" upon the health of the family members.

Occupational level was consistently associated with all-cause mortality cross-culturally. A strong tendency toward a negative association with the cardiovascular endpoints was observed in Rotterdam. When both education and occupation were included in the same analysis, occupation had the stronger association with all-cause mortality. Adjusting for classic risk factors resulted in a slight decrease of relative risks. In Kaunas lower occupational status was no longer significantly associated with mortality, although the tendency still existed (RR = 1.24; 95% CI: 0.96, 1.59). In Rotterdam the relative risk of all-cause mortality remained significant (RR = 1.63; 95% CI: 1.07, 2.48). Status inconsistency and intergenerational mobility had no confounding or modifying effect on the association of SES with mortality. Neither did differences in educational level; the risk of occupation hardly changed when adjusted for education. Hence, socioeconomic differences in mortality were not uncommon in the eastern European part of the KRIS.

The relative absence of an association of SES and CHD (especially in Kaunas) does not correspond with the current literature, which usually reports that the incidence of CHD is elevated in underprivileged groups. This might be because the data were collected during a period in which the gradient between SES and CHD started to change. Several authors have suggested that the SES-CHD gradient may change with time. The rise of the CHD epidemic started in the upper strata and affected all social classes equally at its apex. Thereafter, CHD became more prevalent in the lower strata. If this is true, the gradient necessarily passes a period of zero correlation.

Can the relative absence of the SES-CHD gradient in the KRIS study be explained by the fact that the data were collected during a period in which the gradient started to change? This was investigated by computing the "occurrence of a coronary event" among fathers and their sons in relation to their SES. Among the fathers of the KRIS participants coronary events were usually found among university graduates and those with nonmanual occupations. This was especially so in Kaunas, where fathers who were workers, or who had attended elementary school only, had a risk of a coronary event that was reduced by more than 80%. In the Kaunas cohort the positive association almost disappeared, but not completely. Lithuanians with a low SES had a slightly smaller risk of CHD than Lithuanians with a high SES. In Rotterdam low SES fathers had a significantly reduced risk (approximately 40%) of a coronary event. This gradient reversed in their sons to an increased risk (approximately 60%).

The finding that the SES-CHD gradient actually reversed in the Dutch population suggests that the CHD rates were already declining in the upper social classes in the 1970s. The CHD epidemic in the Dutch population had already passed its apex. It is in this context that, compared to the Lithuanian risk profile, the Dutch profile still consisted of more characteristics typical of modern society. Some examples are: a higher rate of divorce, less stable and less extended social networks, less physical activity, a higher percentage of cigarette smokers and a higher mean cholesterol level.

The belief is expressed (in Sections 1.1 and 4.1) that the SES gradient follows a dynamic pattern and changes with time as a function of the rise and fall of the coronary epidemic. This belief acquires credibility from the data, but no proof. The very proof of this model would require the inclusion of more cohorts and more information about risk factors among fathers and about lifestyle changes in time. This type of investigation is firmly recommended, not only because it would give more insight into the socioeconomic, psychological, and demographic origins of the rise and fall of the coronary epidemic, but also because other more or less lifestyle-related diseases, such as lung cancer, may follow a similar pattern.

Two elements possibly involved in the dynamic pattern of the coronary epidemic might be marital status and geographic mobility. In modern society divorce is increasing, and more people choose to live alone. Divorced men had highly elevated risks of CVD and CHD mortality in Kaunas, whereas single men had the excess risk in Rotterdam. It is likely that sociocultural factors accounted for this difference between Kaunas and Rotterdam. Furthermore, there were some indications that a close social network lowered the risks for the widowed and divorced.

Increasing industrialization may also increase the number of people who leave their sociocultural niche. It was impossible to investigate exactly the health effects of geographic mobility in Kaunas, because almost all participants were born outside Kaunas and moved to that city on an involuntary basis. Rotterdam men born in villages were at increased risk of CVD and CHD, independently of their biological and lifestyle risk factors and of their SES. Detailed analysis shows that the cardiovascular risk tended to decrease, as residence in Rotterdam was extended. This finding clearly points out that geographical mobility gives rise to adaptation processes that increase cardiovascular risk.

Two psychological factors commonly believed to be associated with modernization or industrialization, namely type A behavior and "stress" were not associated with any of the endpoints. This does not refute the type A theory in general. An assessment of type A behavior by questionnaire is less valid than an assessment by interview. The negative finding corresponds with other recently published studies and contributes to the declining attractiveness of the type A theory in general. However, such studies do not prove that the original findings, mainly from the 1960s, were false. Type A behavior possibly exerts its influence mainly during the initial stage of the coronary epidemic, when the initial impact of societal changes causes feelings of loss of control and aggression in unprepared subjects. The slightly elevated mean type A scores of the Lithuanian cohort and the observation by Gostautas (Section 7.9) that type A behavior was predictive of CVD over a longer follow-up period give some support to this belief, but no proof.

Because in Lithuania the replies to the Reeder stress scale were adversely influenced by a response set, the analysis had to be restricted to the Dutch cohort. No associations were observed between the scale scores and any of the endpoints. However, positive results could hardly have been expected because the Reeder stress scale is an outdated instrument. The items of the scale refer to rather different domains. One of them refers to the unusual tiredness that results from prolonged stress ("At the end of the day I am completely exhausted mentally and physically"). This item had good predictive power for CHD mortality occurring during the first years of follow-up. This result fits into the observations made in many retrospective and some prospective studies that a state of exhaustion precedes the onset of CVD (Appels & Mulder, 1988; Appels & Schouten, 1991; Kuller, 1978; Ladwig, 1989). Many cardiologists have been inclined to attribute this association to subclinical heart disease. Recent studies by Carney et al. (1988) and by Kop (1994) show that feelings of exhaustion and lack of energy increase the risk of a new coronary event in patients who have received successful angioplasty (taking all relevant cardiological factors observed during angiography into account). Therefore, these studies support a psychological interpretation of the finding that a state of exhaustion precedes CHD.

An important finding of the KRIS follow-up study is the strong and cross-culturally consistent effect on health of the belief that one's health is poor. Especially those who believed that their health was worse than the health of their peers were at increased risk of all-cause mortality and CVD mortality in both cohorts and of CHD mortality in Rotterdam. Lithuanians were much more pessimistic about their health. The most striking finding of the KRIS follow-up study is the observation that the 30% excess mortality of the Lithuanian cohort could be explained by this pessimistic health perception. This factor also suppressed the advantageous position of the Lithuanian cohort as for the cardiovascular endpoints. Had the Lithuanians been as optimistic about their health as the Dutch, the differences in the incidence of CHD mortality and morbidity would have been even larger.

In section 4.6 it is argued that a pessimistic attitude toward health reflects a low sense of mastery. The positive correlations between health perception and those baseline items that express the feeling that one can do something to protect one's

health support this interpretation. Other interpretations (a negative perception of health reflects subclinical disease, knowledge of parental longevity, or unfavorable socioeconomic conditions) were not supported by the data. These results lead to the recommendation of giving high priority to the investigation of health perception in health psychology and in public health. Health psychology should investigate the elements that do or do not belong to this factor and develop instruments to measure it. Questions that ought to be investigated are: Do comparative questions have more predictive power than self-descriptions (as in this study)? How is this behavior acquired? Does a pessimistic perception of health reflect a negative explanatory style? What are the associations with health behavior, e.g., smoking? As the populations were found to differ considerably in their health perception, public health scientists should investigate the societal origins of a fatalistic perception of health. Questions that ought to be investigated are, for example: Is the health perception in a population associated with characteristics of the health care system? Is a negative perception of health part of a generalized feeling of noncontingency of effort and outcome, which affects other aspects of life as well?

The answer to the question which psychosocial factors influence longevity and increase the risk of CVD mortality can now be summarized as: men from low social classes, men whose wives have a low educational level, nonmarried men and men with self-rated poor health have a reduced life expectancy, independent of their classic risk factors or the culture they live in. Being nonmarried, geographically mobile, having a gloomy outlook on health, and a family history of CVD increase the risk of fatal or nonfatal CHD, independently of the traditional risk factors and the culture in which one lives. Being exhausted increases the risk of CHD as well. However, the cross-cultural consistency of this last factor could not be checked because of technical problems.

How much do psychosocial factors contribute to the identification of high-risk subjects? This question is important for designing cost-effective intervention strategies directed at individuals. ROC curves were selected as the statistical method to answer this question. ROC curves provide information about the increase of the discriminatory power of a set of tests when a new test is added. Originally this method was developed for the evaluation of new diagnostic tests in clinical situations. Because of computational problems, which were mainly caused by empty cells, it was not possible to include all the psychosocial factors in one model together with all the other risk factors. Therefore, ROC curves were computed using a limited number of psychosocial factors (self-rated health, marital status, and parental history of CVD). Due to this reduction the computation of the ROC curves became mainly a methodological exercise.

The results show that, when 1 - specificity = 20% was chosen as an optimal level of specificity, the sensitivity for CHD mortality of age alone was 30% at this point. Adding the psychosocial factors increased this to 41%. Adding the eight biological and lifestyle risk factors to the model increased the sensitivity to 57%. When all risk factors were included in the model, the sensitivity increased to 61%.

This analysis should mainly be considered as a methodological exercise. The numbers give little insight into the relative contribution of the psychosocial factors in the etiology of CHD. Not only is the set of factors included in the analysis rather limited, but psychosocial factors may also affect health through their association with one or more classic risk factors. For example, in Kaunas the mean blood pressure was significantly elevated among those who were born in a small town. Their involuntary migration may have resulted in elevated blood pressure. Adjusting the effect of psychosocial factors for the classic risk factors may be misleading, because in doing so one may adjust a cause for its (intermediate) effect. The association of several psychosocial factors with smoking also points to the environmental determinants of individual lifestyles.

What this suggests for preventive purposes is that psychosocial characteristics can be important in evaluating an individual's risk profile. Knowledge about the social context in which health behaviors and lifestyle originate, develop, and are reinforced can be useful for carrying out public health programs and intervention trials. The relevance of the SES, marital status, and the family culture may be illustrative in this regard. Interventions set up to reduce the level of traditional coronary risk factors could be specifically aimed at people with susceptible positions on any of these environmental characteristics. Intervention programs to change their lifestyle could, then, link up more effectively with the way these groups perceive life. Interventions seem, then, most fruitful, when individuals come to know their own responsibility for their health. Individuals should be made aware of negative health consequences of certain behaviors that are expected and considered appropriate by their peers.

Because not only traditional risk factors were involved in the causal pathway, it is necessary to explore how psychosocial characteristics result in the development of heart disease. The potential importance of more factors was discovered after 1970. Social support, hostility, life events, and lack of control over working conditions or vital exhaustion are such factors, and they may alter the ROC curves. However, in most cases methods of influencing these factors are still being developed. Some of them have been found to be effective in reducing the risk of recurrence in patients afflicted by disease (Friedman et al., 1986). Their efficacy for primary prevention must still be proven, and some of them (family history of CVD, marital status, and SES) can hardly be influenced on an individual level.

SAMENVATTING

Onder auspiciën van de Wereldgezondheidsorganisatie werd in de periode 1972-1974 een cardiovasculair screeningsprogramma gestart in Rotterdam en in Kaunas (een stad in Litouwen; toentertijd één van de republieken van de Sovjet Unie). In de studie, met de naam de Kaunas-Rotterdam Interventie Studie (KRIS), werden vergelijkbare methoden gebruikt om een groot aantal somatische, psychologische en sociologische kenmerken vast te stellen bij 3365 Rotterdamse en 2452 Litouwse mannen tussen de 45 en 60 jaar oud.

Ongeveer tien jaar na de screening bleken 350 Rotterdamse mannen en 303 Litouwse mannen gestorven te zijn. Hiervan waren er respectievelijk 125 en 68 gestorven ten gevolge van een ischemische hartziekte. Daarnaast bleken er 126 en 84 niet-fatale infarcten te zijn opgetreden.

Een zevental psychosociale factoren zijn gedetailleerd onderzocht wat betreft hun potentiële invloed op sterfte en het optreden van een infarct gedurende de tienjarige follow-up:

1. sociaal-economische status
2. sociaal netwerk
3. geografische mobiliteit
4. type A gedrag
5. stress en uitputting
6. subjectief ervaren gezondheid
7. familiale belasting

De analyses werden uitgevoerd met het Cox proportional hazards model ('event history model') en het logistische regressie model. De standaardprocedure was om eerst voor leeftijd te controleren en vervolgens ook de klassieke coronaire risicofactoren (roken, hoge bloeddruk etc.) in het model te introduceren.

Sociaal-economische status

De opleiding van de mannen bleek relatief zwak samen te hangen met de door ons gebruikte eindpunten. Mannen met een laag beroep hadden echter wel een verhoogd risico op vroegtijdige sterfte ten opzichte van mannen met hogere beroepen; dit verband met beroep was zwakker voor het risico op een niet-fataal infarct. Dit laatste was zeker het geval in Kaunas, waar er geen relatie bestond. Dit kan samen hangen met het feit dat ook in de KRIS de relatie tussen sociaal-economische status en ischemische hartziekten tussen twee generaties van richting veranderd is. Dat wil zeggen, bij de vaders van de participanten kwam het infarct vooral voor bij mannen met een hoge sociaal-economische status, terwijl het bij de participanten de neiging vertoont om juist bij de lagere sociale klassen meer voor te komen.

Een andere belangrijke bevinding was dat de opleiding van de echtgenote een sterk effect had op het risico op sterfte c.q. een infarct bij gehuwde mannen. Mannen gehuwd met een vrouw met een laag opleidingsniveau bleken een groter risico te hebben dan mannen met hoog opgeleide echtgenoten. Dit effect was het meest geprononceerd voor de totale sterfte en minder voor de cardiovasculaire eindpunten. Deze samenhang bleek onafhankelijk te zijn van het opleidingsniveau van de man zelf.

Alle bovenstaande relaties berustten slechts ten dele op verschillen in de verdeling van klassieke risicofactoren.

Sociaal netwerk

Burgerlijke staat bleek, onafhankelijk van de klassieke risicofactoren, een sterke relatie te hebben met sterfte en fatale infarcten. Er waren enkele verschillen tussen Nederland en Litouwen in de groepen ongehuwden (nooit gehuwd, weduwnaar en gescheiden) die een speciaal verhoogd risico hadden. In Rotterdam bleken met name de vrijgezellen een verhoogd risico te hebben, terwijl in Kaunas met name de gescheiden mannen en de weduwnaars een verhoogde kans op sterfte hadden.

Alhoewel de gebruikte meting van sociale ondersteuning van vrienden geen hoofdeffect liet zien, werden in beide steden indicaties gevonden voor een beschermend effect van vrienden voor degenen die weduwnaar of gescheiden waren.

Geografische mobiliteit

Geografische mobiliteit was in beide populaties gerelateerd aan een verhoogde kans op een al dan niet fataal infarct. Degenen die ooit van minder geürbaniseerde gebieden naar Kaunas of Rotterdam verhuisd waren, hadden een hoger risico op een infarct dan degenen die altijd in een grote stad gewoond hadden. Dit verhoogde risico had de neiging om te dalen, wanneer men reeds langer in Rotterdam of Kaunas woonde.

Type A gedrag, stress en uitputting

Type A gedrag, vastgesteld met behulp van de Jenkins Activity Survey, bleek geen effect te hebben op de eindpunten. Stress, zoals gemeten door de Reeder stress schaal, had ook geen samenhang met de eindpunten. Omdat de resultaten van de Reeder stress schaal in Kaunas geïnvalideerd waren door een response set, moesten de analyses beperkt worden tot het Rotterdamse cohort. Één item van deze schaal dat specifiek vroeg naar gevoelens van uitputting had een sterk voorspellend vermogen ten aanzien van het optreden van een fataal infarct binnen 1 tot 4 jaar. Ook dit verband kon niet verklaard worden door de klassieke risicofactoren.

Subjectief ervaren gezondheid

Zowel Litouwse als Nederlandse mannen met een als slecht ervaren gezondheid hadden een verhoogde kans op (coronaire) sterfte tijdens de follow-up periode. Verschillende analyses toonden aan dat deze relatie niet gebaseerd was op een reeds aanwezige (subklinische) ziekte. Deze samenhang kon ook niet verklaard worden door familiale belasting of andere risicofactoren. Ook berustte de samenhang niet op het zich zorgen maken over de gezondheid, ongehuwd zijn of een lage opleiding. Nadere analyses maakten duidelijk dat een verklaring mogelijk kan zijn met behulp van de 'sense of mastery' theorie.

Familiale belasting

Het gegeven dat ouders een cardiovasculaire aandoening hadden gehad, bleek in beide populaties samen te hangen met het optreden van een infarct bij de KRIS participanten. In Rotterdam had ook het al of niet voorkomen van cardiovasculaire aandoeningen bij broers of zussen een sterk en onafhankelijk, voorspellend vermogen. Deze familiale clustering van cardiovasculaire aandoeningen en met name de rol van (gedeelde) omgevingsfactoren daarin werd ook geïllustreerd door een sterke samenhang tussen de kansen op een cardiovasculaire aandoening bij beide ouders. Verhoogde bloeddruk en cholesterol gehalte en vergelijkbare opleidings- en beroepsniveaus binnen de familie konden deze samenhang niet verklaren. Vroegtijdige sterfte van de ouders bleek geen relatie te hebben met de eindpunten van de KRIS participanten.

Aparte analyses werden gedaan om de Litouwse en Nederlandse mannen met elkaar te vergelijken. Voor de kenmerken die op eenzelfde manier gemeten zijn in beide steden kon worden vastgesteld dat Rotterdammers ouder waren, eenzelfde systolische bloeddruk hadden, een lagere diastolische bloeddruk hadden, meer rookten, minder alcohol dronken, een hoger cholesterol en glucose tolerantie gehalte hadden, slanker waren en minder lichaamsbeweging hadden dan mannen uit Kaunas. Daarnaast waren Rotterdammers vaker nooit gehuwd of gescheiden en hadden ze vaker ouders, broers of zussen die cardiovasculaire aandoeningen hadden. Tenslotte bleken ze veel vaker hun gezondheid als goed te ervaren dan Litouwers. Deze verschillen tussen de populaties werden gerelateerd aan verschillen tussen de populaties in de kans op sterfte en een niet-fataal infarct. Deze analyses toonden aan dat de Litouwers, rekening houdend met alle risicofactoren, een gunstiger cardiovasculair risicoprofiel hadden dan de Rotterdammers. Dit manifesteerde zich in een verlaagde kans op ischemische hartziekten in Litouwen. Het 30% hoger risico op sterfte gedurende de follow-up in Kaunas kon echter niet verklaard worden door hun risicoprofiel, alhoewel de in het algemeen als slechter ervaren gezondheid in Kaunas een substantiële rol speelde in de hogere mortaliteit in die stad.